UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,377	06/09/2000	ZHONGYI LI	054270/0126	7408

7590 10/24/2002

STEPHEN A BENT
FOLEY & LARDNER
WASHINGTON HARBOUR
3000 K STREET NW SUITE 500
WASHINGTON, DC 20007-5109

EXAMINER
BAUM, STUART F

ART UNIT	PAPER NUMBER
1638	15

DATE MAILED: 10/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/508,377	LI ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-47* is/are pending in the application.

4a) Of the above claim(s) *28,29 and 32-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *23-27,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 July 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group II, claims 23-27 and 30-31 including SEQ ID NO:10 in Paper No. 14 is acknowledged. The traversal is on the ground(s) that the claims of Groups I-IV are drawn to enzymes that by virtue of their involvement in the starch biosynthetic pathway in cereal plants, constitute a "recognized class of chemical compounds" (first page of Applicants' Response to Election) and hence, constitute a single inventive concept.

This is not found persuasive because even though the enzymes are used in a common pathway, proteins are structurally distinct chemical compounds and are unrelated to one another.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 23-47 are pending.

Claims 28-29, and 32-47 are withdrawn from consideration as they are drawn to non-elected material.

Claims 23-27 and 30-31 including SEQ ID NO:10, will be examined on their merits.

Drawings

3. The drawings are objected to for the reasons indicated on the enclosed form PTO-948. Correction is required.

Information Disclosure Statement

4. Two Australian patents listed on form 1449 have not been considered as they were not provided by the Applicant. As stated in the MPEP § 1.98 (a) Any information disclosure

statement filed under § 1.97 shall include: (1) A list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) A legible copy of:

(i) Each U.S. patent application publication and U.S. and foreign patent;

(ii) Each publication or that portion which caused it to be listed.

Specification

5. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

6. Claim 23 is objected to for reading on non-elected material.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 30-31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility.

The Applicants claim a nucleic acid sequence encoding a starch branching enzyme II or biologically-active fragment thereof wherein in the sequence exhibits at least 70% or 90% sequence homology with SEQ ID NO:10.

The Applicants isolated their invention from a cDNA library made from wheat endosperm (page 36, line 23) using the maize branching enzyme I as a probe to pull out homologous sequences. A weakly hybridizing clone was isolated and showed greatest homology to maize branching enzyme II. Using this clone (designated SBE-9), the wheat cDNA library was rescreened and four additional clones were isolated which appeared to be separate fragments of the same gene (page 37, line 7). Sequence analyses suggested that the isolated gene encoded a wheat starch branching enzyme II.

The specification only discloses the specific sequence of SEQ ID NO:10 and asserts that it functions as a starch branching enzyme II (SBE II). However, the functional characteristics assigned to this sequence by Applicant have been determined only by sequence similarity to other SBE II. The specification does not provide any additional information that would support their claims that the functional activity of the disclosed sequence has been established and that the invention is in readily available form for use by those skilled in the art, without the need for further experimentation.

Computer analysis of genome sequences is currently one of the essential steps for obtaining functional and structural information about the respective gene products, but there are a number of inaccuracies that have been documented by researchers in the field. To illustrate the difficulties, Doerks et al., (TIG, 14: 248-250 1998 pg 248, right column, 2nd paragraph) produces a table of BLAST results from an uncharacterized protein family that includes quite a few

proteins with annotations. They state "Only one can give a clue about functional features; others are simply wrong, misleading or uninformative". He continues, "There were even examples in which homologues scored best in PSI-BLAST that did not have the same catalytic activity". It is well established that sequence similarity is not sufficient to determine functionality of a DNA coding sequence. Doerks et al. state that computer analysis of genome sequences is flawed, and "overpredictions are common because the highest scoring database protein does not necessarily share the same or even similar functions" (the last sentence of the first paragraph of page 248). Doerks et al. also teach homologues that did not have the same catalytic activity because active site residues were not conserved (page 248, the first sentence of the last paragraph). In addition, Smith et al (Nature Biotechnology 15:1222-1223, November 1997) teach "there are numerous cases in which proteins of very different functions are homologous" (page 1222, the first sentence of the last paragraph). Also, Brenner (TIG 15, 4:132-133, April 1999) discusses the problem of inferring function from homology, stating "most homologs must have different molecular and cellular functions" (see the second full paragraph of the second column of page 132, for example). Furthermore, Bork et al (TIG 12, 10:425-427, October 1996) teach numerous problems with the sequence databases that can result in the misinterpretation of sequence data. Bork et al discussing the same topic state " search methods are stretched and spurious hits are taken as real. Moreover, similarities might only be restricted to certain domains, but the function is transferred to a whole protein" (pg 426, right column, 1st paragraph). Therefore, neither a credible asserted utility or a well established utility has been established for the claimed invention.

Claims 23-27 and 30-31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Claims 23-27 and 30-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a nucleic acid sequence encoding a starch branching enzyme II which is functional in wheat, or a sequence encoding a starch branching enzyme II that is derived from a *Triticum* species, or a sequence encoding a starch branching enzyme II that is derived from *Triticum tauschii.* The Applicants also claim a nucleic acid sequence encoding a starch branching enzyme II or biologically-active fragment thereof wherein in the sequence exhibits at least 70% or 90% sequence homology with SEQ ID NO:10.

The Applicants isolated their invention from a cDNA library made from wheat endosperm (page 36, line 23) using the maize branching enzyme I as a probe to pull out homologous sequences. A weakly hybridizing clone was isolated and showed greatest homology to maize branching enzyme II. Using this clone (designated SBE-9), the wheat cDNA library was rescreened and four additional clones were isolated which appeared to be separate fragments of the same gene (page 37, line 7). Sequence analyses suggested that the isolated gene encoded a wheat starch branching enzyme II.

The Applicants do not identify structural features unique to the starch branching enzyme II protein, the functional domains of the protein nor the overall function of the protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Given the lack of description for the starch branching enzyme II protein, it remains unclear what features identify any starch branching enzyme II protein or nucleic acid sequence, including a starch branching enzyme II gene or a biologically-active fragment thereof with at least 70% or 90% homology to SEQ ID NO:10. Since a starch branching enzyme II protein has not been described by specific structural features or by specific function, the specification fails to provide an adequate written description to support the generic claims.

9. Claims 23-27 and 30-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a nucleic acid sequence encoding a starch branching enzyme II which is functional in wheat, or a sequence encoding a starch branching enzyme II that is derived

from a *Triticum* species, or a sequence encoding a starch branching enzyme II that is derived from *Triticum tauschii.* The Applicants also claim a nucleic acid sequence encoding a starch branching enzyme II or biologically-active fragment thereof wherein in the sequence exhibits at least 70% or 90% sequence homology with SEQ ID NO:10.

The Applicants isolated their invention from a cDNA library made from wheat endosperm (page 36, line 23) using the maize branching enzyme I as a probe to pull out homologous sequences. A weakly hybridizing clone was isolated and showed greatest homology to maize branching enzyme II. Using this clone (designated SBE-9), the wheat cDNA library was rescreened and four additional clones were isolated which appeared to be separate fragments of the same gene (page 37, line 7). Sequence analyses suggested that the isolated gene encoded a wheat starch branching enzyme II. Applicants have not reduced to practice their invention. They have not taught any plant exhibiting a modified starch polymer as a result of introduction of exemplified or non-exemplified SBE II and they have not taught a modified starch polymer produced in any in vitro system wherein the system comprised an exemplified or non-exemplified SBE II enzyme.

Altering the content or composition of starch by modulating the activity of an enzyme involved in the catabolism or metabolism of starch does not always lead to the expected result. Kossmann et al (1995, Carbohydrate Bioengineering, S.B. Petersen, B. Svensson and S Pedersen (Eds). Pages 271-278) teach that reducing the activity of granule bound starch synthase (GBSS) by antisense technology in potato did not effect the content or composition of starch, even though GBSS is involved in starch metabolism (page 275, paragraphs 4 and 5). Willmitzer et al (1993 In Plant Polymeric Carbohydrates; International Symposium Meuser, F., D.J. Manners

and W. Seibel (Eds) Starch synthesis in transgenic plants, pages 33-39) teach transforming potato with an antisense construct comprising the 35S CaMV promoter operably linked to the Branching Enzyme (BE) did not alter the total starch content or composition of starch in transgenic potato tubers (page 38, 4th paragraph).

It cannot be predicted by one of skill in the art that nucleic acids that exhibit at least 70% or 90% sequence homology to SEQ ID NO:10 will encode a protein with the same activity as one encoded by SEQ ID NO:10. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and

therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants.

Given the unpredictability of altering the chemical structure of starch using enzymes involved in starch metabolism or catabolism for the reasons stated above; given the lack of examples or guidance of using SEQ ID NO:10 or sequences that exhibit at least 70% or 90% sequence homology to SEQ ID NO:10 to alter the branching pattern or chemical structure of starch for the reasons stated above; and given the state-of-the-art that teaches altering the activity of enzymes involved in starch catabolism or metabolism is not predictable, it would require undue experimentation by one skilled in the art to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 23-25 and 30-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Fisher et al (1993, Plant Physiol. 102:1045-1046 including Accession L08065, NCBI Database, 1994).

The claims are drawn to a nucleic acid sequence encoding a starch branching enzyme II or a biologically-active fragment thereof, wherein the sequence is a genomic DNA or cDNA sequence and the sequence is functional in wheat. Applicants have included a proviso that the protein does not include amino acids; AASPGKVLVPDGEDDLASPA.

Fisher et al teach a cDNA sequence that encodes a starch branching enzyme II from maize and it would be functional in wheat. Using the amino acid sequence as listed in the NCBI database, the deposited sequence does not contain the amino acids AASPGKVLVPDGEDDLASPA in the N-terminal region of the sequence and as such, Fisher et al anticipate the claimed invention.

11. Claims 23-26 and 30-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Chibbar et al Proceedings of the International Wheat Quality Conference, Manhattan, Kansas, USA, 18-22 May 1997, pages 249-260).

The claims are drawn to a nucleic acid sequence encoding a starch branching enzyme II or a biologically-active fragment thereof, wherein the sequence is a genomic DNA or cDNA sequence wherein the sequence is derived from wheat and the sequence is functional in wheat. Applicants have included a proviso that the protein does not include amino acids; AASPGKVLVPDGEDDLASPA.

Chibbar et al teach a cDNA sequence that encodes a starch branching enzyme II from wheat and it is functional in wheat and as such, Chibbar et al anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 23-27 and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chibbar et al Proceedings of the International Wheat Quality Conference, Manhattan, Kansas, USA, 18-22 May 1997, pages 249-260).

The claims are drawn to a nucleic acid sequence encoding a starch branching enzyme II or a biologically-active fragment thereof, wherein the sequence is a genomic DNA or cDNA sequence wherein the sequence is derived from *Triticum*, in particular, *Triticum tauschii* and the sequence is functional in wheat.

Chibbar et al teach a cDNA sequence that encodes a starch branching enzyme II from wheat and it is functional in wheat.

Chibbar et al do not teach a starch branching enzyme II from *Triticum tauschii.*

Given the recognition of those of ordinary skill in the art of the value of cloning a SBE II gene or cDNA from a wheat species as taught by Chibbar et al, it would be a matter of choice to choose one species of wheat over another.

Thus the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Sonya Williams, whose telephone number is (703) 305-2272.

Stuart Baum Ph.D.

October 18, 2002

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600